



Vascularised bone grafts for the management of non-union

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KEYWORDS

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Summary Non-union of the long bones may have severe consequences, particularly when combined with other post-traumatic sequelae, such as tendon adhesions, reflex sympathetic dystrophy and infection, among others. In these cases, it is important to treat the delayed union or non-union first or at the same time with the other problems in order to achieve adequate function. Once the normal bony healing process has been slowed or stopped, it is necessary to provide both stability to the fracture site, as well as a biological stimulus for the fibrocartilagenous callus to finish the healing process. Vascularised grafts, such as the free fibula, offer not only structural support, but also promote bone healing. The later is achieved by trabecular bone formation, as well as vascular sprouting from pedicle vessels.

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Introduction

The metaphysis of long tubular bones is comprised primarily of trabecular bone or spongiosa, while the diaphysis contains mostly cortical or lamellar bone. As a result, fracture healing in these complex bony structures is a multifaceted phenomenon. In general, the healing process is initiated principally by the organisation of a blood clot around and between

the fracture ends. Eventually, cells originating from the periosteum and endosteum, as well as perivascular cells begin to populate the clot. Subsequently, a wide variety of factors, including mechanical (compression–tension), ionic conditions, pH variations, hormonal factors, play significant roles in the transformation of the initial blood clot to mature bone.⁶¹

Three phases have been described for fracture healing when there is no surgical intervention. First, is the inflammation phase, which lasts about 10% of the healing time. Secondly, is the reparative phase, which comprises 40% of the healing time and during which the clot is transformed to a mineralised callus

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which bridges the fractured ends. Lastly, is the remodelling phase, which is a slow and long process that comprises about 70% of the healing process. During this phase, which may take years, the ununited fractured bones are slowly transformed back to normal bone.⁸

Eventually, the initial clot is transformed to callus comprised of fibrocartilage and then to bone by intramembranous and endochondral ossification. Thus, initially woven bone is formed which is subsequently transformed to cortical bone by apposition of the lamellar bone. This type of healing is referred to as secondary healing and occurs when the fractured ends were not initially rigidly stabilised and were not placed under compression. On the other hand, when the fractured bone has been stabilised using the AO principles of internal fixation of fractures with rigid fixation and compression, a direct or primary fracture healing occurs. In primary fracture healing, no cartilage formation is found in the fracture site. Moreover, no visible callus formation is detectable and the fracture line disappears with time.⁶¹

Many factors may delay or even stop the healing process either leading to extensive fibrocartilage formation in secondary healing or resulting in the formation of fibrocartilage in primary healing. Once this dense tissue fills the fracture site, delayed union or non-union occurs. Among the factors, which have been identified as unfavourable for bone healing, include extensive trauma, bone loss, unstable fixation premature mobilisation, infection, extensive osteonecrosis and old age.⁵⁷

Fracture non-union and delayed union remain serious problems with substantial morbidity.²⁸ As wound healing is dependent, among other factors, on local tissue vascularity, vascularised bone grafts have been proposed as a means of managing non-union providing means to further assist the healing process by improving the cell-deficient and poorly vascularised environment.

Delayed union and non-union: the role of vascularity

Delayed union is defined as an abnormal slowing of the fracture healing process, which nonetheless will continue to completion with time. Non-union, on the other hand, is defined as a complete cessation of the healing process after about 6–9 months. Thus, the healing process stops in an incomplete state with no potential for complete bony healing to place without intervention.

Radiologic signs of fracture healing may take up to 12 months before becoming evident. Moreover, radiologic signs often appear considerably later than

clinically healing. In this regard, the diagnosis of delayed union or non-union is often ambiguous. This, in turn, has resulted in some controversy regarding the time that non-union or delayed union should be diagnosed. Debate on the time elapsed before the diagnosis of delayed union or non-union can be made, is complicated further by the fact that prolonged immobilisation of a delayed union may compromise the functional result. Clinical signs of non-union include motion at the fracture site and pain, while radiographic signs include persistent fracture lines with bone sclerosis, hypertrophic callus formation or atrophic callus formation with bone resorption.

An inadequate blood supply of the fracture site is a primary contributor to the development of delayed union and non-union. Blood supply can be negatively affected by the initial injury, which, in turn, can affect the outcome of the fracture. Thus, extensive trauma, comminuted fractures, damage of the nutrient artery at the time of injury or later as a result of manipulation, large bony defects, excessive periosteal stripping and insufficient stabilisation may lead to delayed union and non-union.⁵⁶

Atrophic non-union is usually attributed to an impaired blood supply. In an animal model of atrophic non-union, investigators assessed the number of blood vessels at the site of an osteotomy using immunolocalisation techniques in both normally healing bones and in atrophic non-union.³² One week post-operatively, significantly fewer blood vessels were observed in the non-union group, although by 8 weeks the number of vessels had reached the same level as that in the healing group. This findings support the hypothesis that the number of blood vessels in atrophic non-union reaches the same level as that in healing bone, but at a later time-point. In turn, this suggests that early enhancement of diminished vascularity may help prevent non-union of fractures.

Open fractures, high energy and degloving injuries may also be predisposed for delayed union or non-union. This predisposition has been attributed to, in part, to a decreased activity of the fracture exudates, which contains growth factors, such as PGG2, among others.³⁰ Finally, diaphyseal fractures are more prone to non-union than epiphyseal fractures. This is attributed to the type of bone which is predominately found in these anatomical regions. More specifically, cortical bone, which is located in diaphysis has fewer cells per volume compared to cancellous bone.⁸⁰

Vascularised bone grafts: general issues

Bone grafts are an important part of orthopaedic surgeon's armamentarium. In the extremities, bone

grafts are used for the treatment of non-unions and necrotic lesions, for skeletal structural support and for the reconstruction of defects resulting from trauma, tumor excision, osteomyelitis, congenital pseudarthrosis or radiation necrosis. In all cases, their use is successful provided that the host bed has adequate vascularisation. In cases of decreased blood supply, the choice of a vascularised bone graft seems inevitable, as bone grafts with intrinsic blood supply lead to higher success rates and to acceleration of the repair process in the reconstruction of defects and necrotic lesions of the skeleton.^{1,4,44-47} The additional advantage of harvesting vascularised bone grafts in combination to skin and/or muscle offers solution to complex problems in skeletal/soft-tissue defect reconstruction.

Vascularised grafts can be classified according to their structure (cortico-cancellous bone, periosteum, epiphysis, joint), size (large, small), donor site (fibula, iliac crest, rib, scapula, distal radius, carpal bones, metacarpals), need for anastomosis (free, pedicled) and combination to other tissues (simple, composite).

The decision to use a free versus a pedicled graft depends upon the location of the recipient site and the potential donor sites in the region, the length of the pedicle and the arc of rotation (to allow approach of the vascularised bone graft to the recipient site in order to bridge the defect),¹⁴ as well as the diameter of the vessels (severe discrepancy between the donor and recipient site vessels, or very small dimensions of pedicles may prohibit the anastomosis). The use of a pedicled graft, harvested from sites nearby the recipient, limits the surgical approach and decreases the length of the procedure due to the absence of anastomoses.

Larger grafts (fibula, iliac crest, rib, scapula) may be combined with skin (osteocutaneous) and/or muscle (osteomuscular graft) that are nourished by perforators through the same pedicle that nourishes the bone graft. Composite grafts provide coverage of bone and soft-tissue defects of the extremities. The most commonly used composite graft is the fibular graft combined with soleus or the flexor hallucis longus muscle and the skin.

Apart of vascularised bone grafts other structures may be transferred, such as the periosteum, the epiphyseal plate, as well as an entire joint.

Vascularised periosteal flaps

Vascularised periosteum is an elastic and flexible membrane with known osteogenic properties that is adaptable to the shape of the recipient area.^{76,9} Recent experimental studies showed that the vascularised periosteum is a promising alternative for

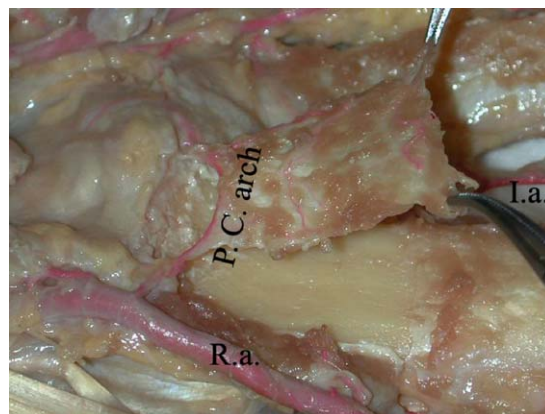


Figure 1 Vascularised periosteal graft from the palmar aspect of the distal radius. The graft is based on the palmar carpal arch (between the radial and the anterior interosseous artery) (Ra, radial artery; PC arch, palmar carpal arch; Ia, anterior interosseous artery).

the reconstruction of small skeletal defects.^{13,58,77} The periosteum is able to guide new bone formation and prefabricate bone that is adapted to the recipient defect (Fig. 1).^{73,78}

The use of vascularised periosteum in skeletal defect reconstruction has negligible donor site morbidity.⁷ Multiple donor sites have been described, including iliac crest, distal femur, tibial shaft, fibula, 10th rib, scapula, distal humerus, radius and ulna.^{11,16,54,14} The vascularised periosteal flap has been successfully applied in the upper extremity for scaphoid non-union, Kienbock's disease, wrist arthrodesis and defects of metacarpals and phalanges.^{16,14} Vascularised periosteum has also been used in the lower extremity,¹¹ the mandible, as well as for avascular necrosis of the talus¹⁶ and femoral head.⁷⁹

Vascularised epiphyseal platetransfer

Vascularised epiphyseal plate transfers offer several advantages for the reconstruction of defects of the growing skeleton, particularly for distal radial defects. Donor sites include the iliac crest, scapula and proximal fibular epiphysis.⁷¹ The proximal fibular epiphysis also offers a joint surface. The transfer of proximal fibular transfer is based on the anterior tibial artery. It provides not only skeletal and joint reconstruction, but also growth potential, as 70% of the fibular growth is expected from the proximal epiphyseal plate.^{31,32}

Free vascularised joints

Free vascularised joints have been used in hand surgery. Free vascularised metatarsophalangeal

(MTP) joint is based on the dorsal interosseous artery. It may be transferred to the metacarpophalangeal joints, whereas the second toe proximal interphalangeal (PIP) joint which based on the plantar digital artery, may be used to replace a damaged PIP joints of the hand.^{65,20,63} Vascularised joints may be also used from non-replantable digits for the reconstruction of complex hand injuries.²⁷

Treatment of delayed union and non-union: the use of vascularised bone grafting

Once the normal fracture healing process has been slowed or stopped, two conditions are necessary in order to establish union. One requirement is stability, which can be achieved by internal or external fixation. The second prerequisite is a biological stimulus for the fibrocartilagenous callus to finish the healing process. One such biologic stimulus is bone graft material. In this regard, fresh autologous bone grafts, particularly cancellous bone, have osteogenetic properties from the cells, which survive the procedure. Osteoconduction reflects the ability of a bone graft to act as a scaffold, where osteoblasts from the host are able to synthesise bone through the process of creeping substitution.¹⁷ Osteoconduction, therefore, is the ability of the bone graft to induce bone formation in the bone bed of the lost.

Stability is also a key factor in treating non-unions and it may be achieved by various methods. In most cases of non-union, the treatment of choice is the freshening of the non-united ends with the application of bone grafts followed by stabilisation with internal or external fixation. In cases of non-union related to bone loss and shortening, it is essential to re-establish the bony length for better function of the tendons. This may be achieved by a lengthening procedure using an external fixation device. Once the optimal length has been achieved, then a bone graft, frequently a corticocancellous graft from the iliac crest, can be used to cover the defect. The external fixator may be left in place until full consolidation of the graft.

It is clear that the factors which contribute to delayed union or non-union are complex. Generally, contributing factors can be divided into three major categories: deficiencies in vascularity, deficiencies in the robustness of the chondroosseous response and deficiencies in stability. For a bone graft to enhance bone healing, it must help alleviate the primary causing factor. The various types of grafts used today, ranging from autogenous fresh cancellous to cortical bone and free vascularised grafts,

have demonstrated varying capacities to induce active bone formation or to serve as a substrate for bone formation. These capacities are tightly dependent upon the surrounding environment, particularly the mechanical and vascular environment.⁶⁹

The timing and intensity of the immune response differ according to whether a vascularised or non-vascularised graft is being used. Vascularised bone allografts generate significant cell-mediated and humoral responses early on.³⁴ Experimental findings, such as these support the hypothesis that clinical application of vascularised bone allografts may offer significant advantages over non-vascularised allografts in the reconstruction of massive bone defects. Complications, such as non-union, fracture and collapse of articular segments seen in non-vascularised transplantation may be avoided by preservation of the blood supply to the graft.

Large vascularised bone grafts

Vascularised bone grafts, including fibula, iliac crest, ribs and scapula, have been used to manage recalcitrant post-traumatic shaft non-union of long bones. The vascularised fibular graft can be effectively used for patients with large bony defects and with poor intrinsic stability of the non-union site.^{45,47,52} In atrophic non-union without a substantial bone defect, particular of the long bones of the upper extremity, a corticoperiosteal femoral graft can also provide satisfactory results.

Pedicle vascularised bone grafts enables the transfer of bone with preserved circulation and viable osteoclasts and osteoblasts. A useful example is the reverse-flow pedicle vascularised bone graft from the dorsal distal radius.⁶⁴ This type of grafting procedure allows for primary bone healing without creeping substitution within the dead bony tissue, and assists in promoting the healing process, replacing deficient bony tissue and revascularising ischemic bone. Advances in the understanding of the anatomy of vascularised pedicle bone grafts have enabled their successful application in managing a variety of carpal disorders, including scaphoid non-unions and Kienbock's disease.⁶⁴

Free vascularised fibular graft

Free vascularised fibular grafting has been proven a valuable tool in the armamentarium of the orthopaedic surgeon, particularly in managing aspectic or infected non-unions with an impressive success rate.^{24,45,47} In most cases, these non-unions are complicated with previous surgical procedures,

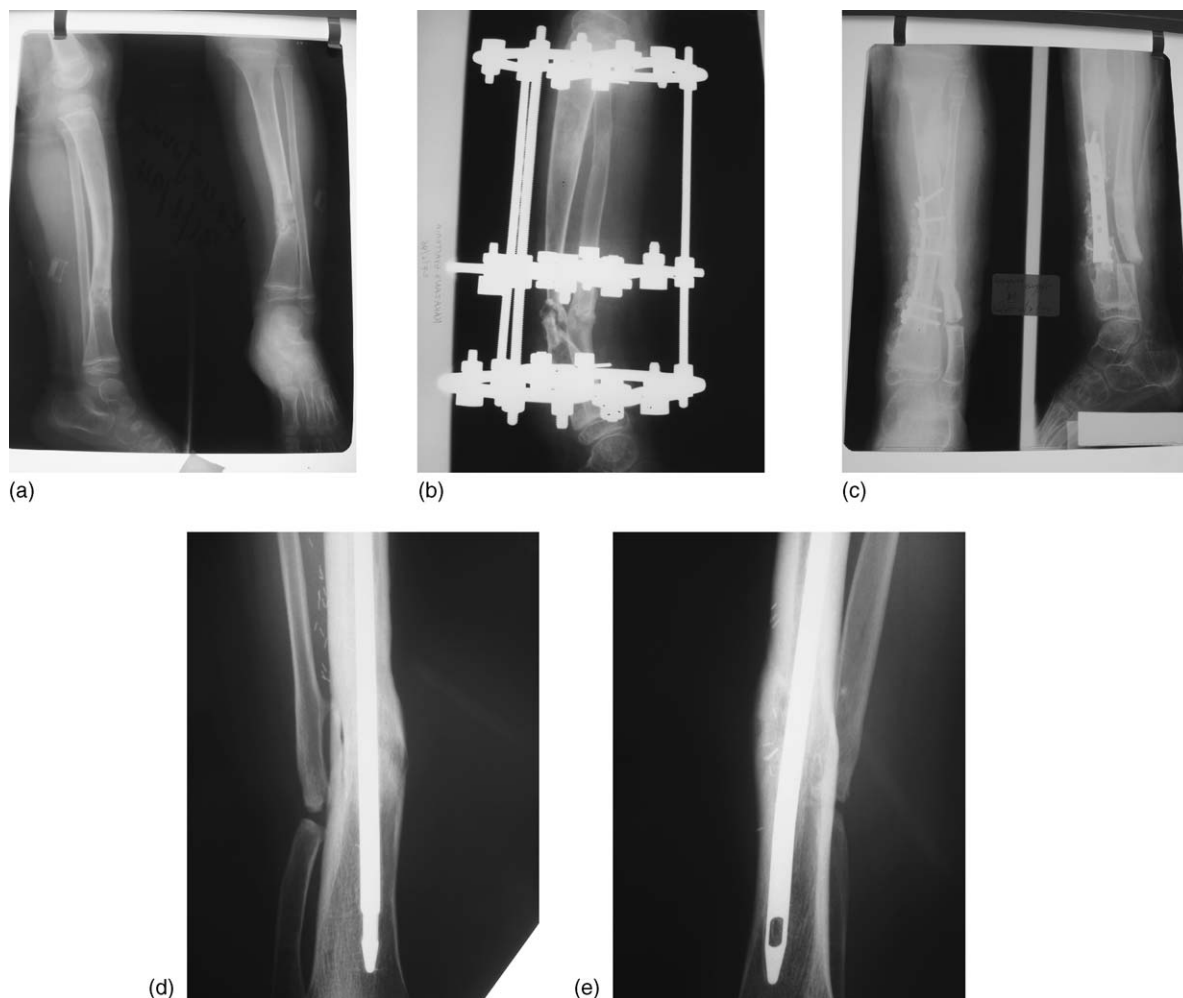


Figure 2 (a) Congenital pseudoarthrosis of the distal third of the tibia in a 3-year-old girl. (b) Various surgical procedures, all of which failed, were attempted to treat the congenital pseudoarthrosis of the tibia. Shown here is an external Ilizarov fixator that was attempted at age 5 years and which also failed. (c) After the previous failures, a vascularised fibular graft was used to treat the pseudoarthrosis (age 7 years). (d) Anteroposterior and (e) lateral radiographs showing complete healing and remodelling of the tibia with full incorporation of the fibular graft 7 years postoperatively. The IM nailing was used to treat a recent proximal fracture of the tibia.

bone atrophy, damage to the surrounding soft tissues, as well as focal infection. These problematic cases require thorough bone and soft tissue debridement, before bridging of the bony defect with the vascularised fibula graft. Various modalities of internal fixation can be used, depending on the host bone. It is important to note, however, that with vascularised fibular grafting, careful monitoring of circulation and early intervention surgery is necessary to avoid vascular failure (Fig. 2).

With the use of free vascularised fibula grafting, Safoury successfully managed infected non-unions and segmental defects of both the radius and ulna that had failed to resolve with conventional treatment.⁶⁰ The ipsilateral fibula was used as an osseous or osseocutaneous free flap to reconstruct the radial, but not the ulnar, continuity. Reconstruction of the radius provided a stable forearm, and use of

the vascularised fibula graft enable fracture union with good soft-tissue healing and resolution of infection. Vascularised bone grafts, including fibula, femur and scapula, were also effectively used to treat patients with recalcitrant post-traumatic humeral shaft non-union.⁵⁰

Vascularised iliac crest

The iliac crest bone graft, is a cortico-cancellous graft, based on the deep circumflex iliac artery and it is mainly used as a free graft. Because its shape is not adaptable to the long bones of the extremities or the smaller bones of the hand and wrist, it has relatively restricted applications. However, the free vascularised iliac crest has been used for the treatment of scaphoid non-unions (free vascularised or conventional graft) combined with vascular bundle

implantation into the non-union^{53,21,19} and the reconstruction of skeletal defects of the upper and lower extremity.^{26,39} The use of a pedicled iliac crest graft has been described for femoral head necrosis and acetabular reconstruction in total hip replacements.^{37,18}

Vascularised scapular and rib grafts

Similar to the iliac crest, the vascularised scapular graft is a cortico-cancellous graft with limited applications because of its shape. Although the majority of applications of both iliac crest and scapula grafts are for mandibular reconstruction,³⁵ there are some sporadic reports that describe the use of vascularised scapular grafts in the extremities.^{70,82,71}

The rib is a weak, membranous bone with curved shape. As a free vascularised graft (based on the intercostal vessels) the rib presents very limited applications: restoration of hindfoot, reconstruction of post-traumatic and congenital defects and spinal fusions.^{1,6,36,43,51,72,75}

Small vascularised bone grafts

Small vascularised bone grafts are commonly used for the treatment of wrist problems (scaphoid non-unions, osteonecrosis of proximal scaphoid and lunate). They are also indicated for the treatment of skeletal defects of the hand, resulting from trauma or infection.⁵⁹

Several authors have described the vascular anatomy and the donor sites of the distal radius, ulna and second metacarpal.^{23,62,14,55} Many pedicles have been identified of the dorsal distal radius (1,2 intercompartmental artery; 2,3 intercompartmental artery; fourth extensor compartment artery), palmar distal radius (palmar carpal arch and palmar metaphyseal arch) and dorsal hand (first dorsal metacarpal artery second, third and fourth dorsal metacarpal arteries) with lengths ranging between 0.5 and 3 cm. Pedicles are usually raised with a periosteal strip and/or muscle and their arc of rotation provides dorsal approach to the distal half of the forearm, the wrist and hand to the proximal interphalangeal joints (PIP) and palmar approach to the lower third of the forearm and the wrist.

Distal radius pedicle

The pedicles of the bone grafts harvested from the distal radius have sufficient length for rotation and transition to the carpal bones. In the treatment of scaphoid non-unions the bone graft must have ade-

quate dimensions to fill the gap and restore scaphoid length and specific shape to restore the angulation of the scaphoid, apart of the intrinsic vascularity that will enhance healing-in most series vascularised bone grafts lead to union in 6–12 weeks.^{38,44}

The site of the non-union is critical for the selection of the most appropriate bone graft. For the reconstruction of non-unions of scaphoid waist, grafts from the palmar-ulnar aspect of the radial metaphysis, which are based on the palmar carpal artery running on the distal edge of pronator quadratus can be used.³⁸ For non-unions of the proximal third of the scaphoid, grafts from the dorsal–radial side of the distal radius have been successfully applied.^{83,44,68} Finally, bone grafts based on the dorsal wrist capsule⁶⁶ and on the ulnar artery²⁵ may be also used for the treatment of scaphoid non-unions.

In Kienbock's disease vascularised bone grafts have been used for the reconstruction and revascularisation of the lunate. The grafts from the distal radius may be palmar (based on the palmar carpal artery) or dorsal (based on the arteries of the fourth and fifth extensor compartments).^{48,49,59,64}

Vascularised carpal bone and metacarpal grafts

Vascularised bone grafts from the scaphoid tubercle and the pisiform may be used for the treatment scaphoid non-unions and for the replacement of the lunate in Kienbock's disease.^{33,12} Grafts from the second metacarpal, pedicled on the first dorsal metacarpal artery may be used for defects of the distal radius, carpal bones, metacarpals or phalanges.¹⁴

Management of non-union in a deprived biological environment: non-union of femoral neck fractures complicated with osteonecrosis

Due to the anatomy of the blood supply to the femoral head as well as contributing biomechanical factors, femoral neck fractures are associated with high complication rates and present a challenge to the orthopaedic surgeon. This is especially true when dealing with patients younger than 50 years old, with whom every attempt should be made to avoid or delay hip arthroplasty.^{3,10} This age group, however, presents the highest rates of non-union and osteonecrosis, as the high-energy trauma involved usually leads to significant displacement and a relatively vertical fracture plane.⁸⁴ The rates

reported in the literature for development of non-union and osteonecrosis in young patients with femoral neck fractures vary widely, although can reach as high as 86%.

It is well known that non-union and osteonecrosis of the femoral head frequently complicate intracapsular femoral neck fractures, hence the term "unsolved fracture" coined by Speed,⁶⁷ and "unsolvable fracture" later used by Garden.²² This is especially true in young patients, where high-energy trauma is usually involved, leading to increased displacement and shearing forces.⁸⁴ Treatment with reduction and internal fixation in this patient population is associated with a 0–59% rate of non-union and 19–86% rate of osteonecrosis.^{15,74,84} A variety of procedures have addressed the biological factor with use of non-vascularised bone grafts, muscle pedicle vascularised bone grafts, pedicled vascularised bone grafts and free vascularised fibular grafts.^{2,4,5,29,40,42,60} The results reported in the literature with use of the existing techniques have been variable.

Simple reduction and internal fixation has been described as a viable solution in selected patients with femoral neck non-union. Wu et al.⁸¹ reported treatment of 11 patients; all non-unions healed after a mean period of 4.6 months, and no osteonecrosis or other complications occurred during a minimum follow-up of 2 years. However, all patients were selected for this procedure after bone scanning had revealed absence of avascular necrosis of the femoral head.

Procedures attempting to revascularise the femoral head have been used in the management of patients with post-traumatic osteonecrosis, or for primary surgery on patients with a high probability of avascular necrosis. These procedures include non-vascularised bone grafting, muscle-pedicle bone grafting, pedicled vascularised bone grafting, and free vascularised fibular grafting.

The poor results reported with use of avascular grafts led to the use of vascularised grafts. A union rate of 72% was reported. Baksi² reported use of a muscle pedicle bone graft for treatment of 56 patients with non-union, neck absorption and evident avascular necrosis in 34 cases. Their procedure consisted of non-union site takedown, femoral head decompression, internal fixation and introduction of the muscle pedicle bone graft. They reported satisfactory union in 75% of patients, which reached 82%, if delayed union was included. Femoral head collapse occurred in 6% of the patients with osteonecrosis. Mechanical failure was noted in 16% of cases. Union was achieved in three cases with an adjunctive osteotomy, an indication that vascularised bone grafts and osteotomy, used in combination in our

study, may play complimentary roles in this clinical situation.

The finding that blood supply of muscle pedicle bone grafts is unreliable, led to the use of vascularised pedicled bone grafts. Leung and Shen^{41,42} described use of a pedicled bone graft from the iliac crest in treatment of 15 patients with femoral neck fractures. Of these only two had non-union, two had delayed union and the rest were neglected fractures. None of the patients had evident osteonecrosis preoperatively. The bone graft was placed with press-fit technique in a trough that traversed the fracture site. Union was achieved in all 15 patients. A similar technique, with the addition of screw fixation of the graft, was used by Hou et al.²⁹ to treat five patients with neglected fractures. Of these, only two patients had non-union and bone scanning revealed no osteonecrosis. Union was achieved in all five patients within 5 months. This procedure provides the advantages of a vascularised bone graft, without requiring microsurgical anastomoses. The results of these studies, while very satisfactory, cannot be directly compared to ours, as they mainly concern primary treatment of neglected fractures, without the complication of avascular necrosis.

Later, LeCroy et al.⁴⁰ published the first report of use of free vascularised fibular grafts in this patient group. They treated 22 consecutive patients with femoral neck non-union and femoral head osteonecrosis after failed internal fixation. Non-union site takedown and correction of neck shaft angle were achieved during reaming and coring of the femoral neck in preparation for the fibular graft. Knowles pins or cannulated cancellous screws provided additional fixation in all cases. They reported very satisfactory results, with union being achieved in 91% of cases (20 out of 22) after a mean period of 9.3 months. The remaining two consolidated after a second procedure involving pedicled vascularised grafting.

The vascularised fibula, placed subchondrally, provides structural support to the articular surface. Revascularisation of the femoral head and bone healing are promoted by trabecular bone formation, as well as vascular sprouting from the pedicle vessels.²⁵ We have operated on five patients (four males and one female) with non-union of traumatic femoral neck fractures and concomitant osteonecrosis of the femoral head using a combination of subtrochanteric valgus osteotomy, internal fixation and free vascularised fibular grafting.⁴ The patients had a mean age of 26.6 years (range 16–37 years) and the mechanism of injury was a motor vehicle accident in all five cases. The femoral neck fracture was subcapital in two patients, transcervical fracture in another two, and a basilar neck fracture in

one case. All patients had received initial treatment at other centers. At the time of referral (range 6–16 months), all patients presented with non-union and osteonecrosis of the femoral head. Patients were available for follow-up for a mean period of 65.2 months (range 51–74 months). Osseous union was achieved in all five patients after a mean period of 5.6 months (range 4–8 months). No adjunctive procedures were necessary to achieve union. There were no cases of hardware migration. Progression of osteonecrosis was arrested in three cases.

The achievement of union was associated with a significant decrease in hip joint pain and an improvement of range of motion. Range of motion was near normal in three cases and satisfactory in the remaining two. No significant morbidity was associated with the donor site in any of the patients. In the patient who received a non-vascularised fibular graft, union was also achieved after a period of 8 months, with no progression of the osteonecrosis. The result in the patient with the pathological fracture was excellent as well. Union was achieved within 6 months, with filling out of the cystic space and preservation of the femoral head.

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